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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,630	05/30/2006	Kari Alitalo	28113/39467A	2853

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EXAMINER	
BOWMAN, AMY HUDSON	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
12/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,630	ALITALO ET AL.	
	Examiner	Art Unit	
	AMY BOWMAN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-15, 17, 21, 22, 25-29, 31, 33, 34, 36-38, 41, 46, 48, 52, 54, 55, 68, and 70-76* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-15,17,21,22,25-29,31,33,34,36-38,41,46,48,52,54,55,68 and 70-76.

DETAILED ACTION

Election/Restrictions

It is noted that the previous election/restriction requirements mailed on 1/15/08 and 8/19/08 inadvertently failed to treat the application as a national stage entry of PCT/EP04/08819 and were incomplete. Therefore, the previous election/restriction requirements are hereby withdrawn and the instant election/restriction is pending.

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-6 and 11-15, drawn to a method of screening colon tissue for a pathological condition via measuring Prox-1 protein expression. **Election of this group requires election of one further measurement steps from claims 11 and 12. Should applicant elect the species of claim 12, applicant is further required to elect one species from claim 13, as explained below.**

Group II, claim(s) 1-4 and 7-15, drawn to a method of screening colon tissue for a pathological condition via measuring Prox-1 mRNA expression. **Election of this group requires election of one further measurement steps from claims 11 and 12. Should applicant elect the species of claim 12, applicant is further required to elect one species from claim 13, as explained below.**

Group III, claim(s) 17, 21, 22, 25-29, 31, 33, 46, 68, and 70-76, drawn to a method of inhibiting the growth of colorectal cancer cells via administering a composition that suppresses the expression of Prox-1 to a subject, further comprising administering to the subject an inhibitor of DNA methyltransferases. **Election of this group requires election of one type of molecule from claim 22, 26, 27, 68, or claim 74. If applicant elects "siRNA", applicant is required to elect one sequence from claim 25. If applicant elects a "molecule that comprises a dominant negative form of Prox-1 protein", applicant is required to elect one species from claims 28 or 29. If**

applicant elects "antisense oligonucleotide", applicant is further required to elect one species of target regions from claims 71-73, as explained below.

Group IV, claim(s) 17, 21, 22, 25-29, 31, 33, 34, 36, 37, 46, 68, and 70-75, drawn to a method of inhibiting the growth of colorectal cancer cells via administering a composition that suppresses the expression of Prox-1 to a subject, further comprising administering to the subject an inhibitor of the β-catenin/TCF signaling pathway. **Election of this group requires election of one type of molecule from claim 22, 26, 27, 68, or claim 74. If applicant elects "siRNA", applicant is required to elect one sequence from claim 25. If applicant elects a "molecule that comprises a dominant negative form of Prox-1 protein", applicant is required to elect one species from claims 28 or 29. If applicant elects "antisense oligonucleotide", applicant is further required to elect one species of target regions from claims 71-73, as explained below. Election of this group also requires further election of one species from claims 36 or 37, as explained below.**

Group V, claim(s) 17, 21, 22, 25-29, 31, 33, 38, 46, 68, and 70-75, drawn to a method of inhibiting the growth of colorectal cancer cells via administering a composition that suppresses the expression of Prox-1 to a subject, further comprising administering to the subject a COX-2 inhibitor. **Election of this group requires election of one type of molecule from claim 22, 26, 27, 68, or claim 74. If applicant elects "siRNA", applicant is required to elect one sequence from claim 25. If applicant elects a "molecule that comprises a dominant negative form of Prox-1 protein", applicant is required to elect one species from claims 28 or 29. If applicant elects "antisense oligonucleotide", applicant is further required to elect one species of target regions from claims 71-73, as explained below.**

Group VI, claim(s) 17, 21, 22, 25-29, 31, 33, 41, 46, 68, and 70-75, drawn to a method of inhibiting the growth of colorectal cancer cells via administering a composition that suppresses the expression of Prox-1 to a subject, further comprising administering to the subject a Notch signaling pathway agonist. **Election of this group requires election of one type of molecule from claim 22, 26, 27, 68, or claim 74. If applicant elects "siRNA", applicant is required to elect one sequence from claim 25. If applicant elects a "molecule that comprises a dominant negative form of Prox-1 protein", applicant is required to elect one species from claims 28 or 29. If applicant elects "antisense oligonucleotide", applicant is further required to elect one species of target regions from claims 71-73, as explained below.**

Group VII, claim(s) 48, 52, 54, and 55, drawn to a method of screening for a Prox-1 modulator.

The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

37 CFR 1.475(b) states:

"An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn **only** to one of the following combinations of categories:

(1) A product and a process specially adapted for the manufacture of said product; or

(2) A product and process of use of said product; or

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

37 CFR 1.475(c) states:

"If an application contains claims to more or less than one of the combination of categories of invention set forth in paragraph (b) of this section, unity of invention might not be present."

37 CFR 1.475(d) also states:

"If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) and 1.476(c)."

37 CFR 1.475(e) further states:

"The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternative within a single claim."

The instant claims are directed to multiple processes and therefore do not fall into any one of the only 5 combinations of categories which can have unity of invention as defined by 37 CFR 1.475(b). Therefore, by definition of this rule, there is no unity of invention.

This application contains claims directed to the following patentably distinct species of measurement steps in claims 11-13: measuring expression of at least one gene; or measuring activation of β-catenin/TCF pathway. The species are independent or distinct because each of the steps measure completely different molecules, each method requiring separate and distinct search considerations. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 1 is generic.

It is noted that should applicant elect measurement of at least one gene, as recited in claim 11, applicant is further required to elect one gene from claim 11, as each gene is structurally distinct, each requiring a separate and distinct search and corresponding examination.

Should applicant elect measuring activation of β-catenin/TCF pathway, applicant is required to elect one species of indicators from claim 13, as each represents a separate and distinct embodiment of the instant method.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

Additionally, claims 36 and 37 are drawn to multiple inhibitors of the β-catenin/TCF signaling pathway; and claims 22, 25-29, 68, and 71-74 are drawn to a multitude of inhibitory molecules. According to the guidelines in Section (f)(i)(a) of Annex B of the PCT Administrative Instructions, the special technical feature as defined by PCT Rule 13.2 shall be considered to be met when all the alternatives of a Markush-group are of similar nature. For chemical alternatives, the Markush group shall be regarded as being of similar nature when

> (A) all alternatives have a common property or activity and; (B)(1) a common structure is present, i.e., a significant structure is shared by all of the alternatives; or (B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to an art-recognized class of compounds in the art to which the invention pertains.

The instant inhibitors of the β-catenin/TCF signaling pathway of claims 36 and 37; and inhibitory molecules of claims 22, 25-29, 68, and 71-74 each result in methods that are each separate inventions for the following reasons: The inventions do not meet the criteria of (A), common property or activity or (B)(2), art recognized class of compounds. The inhibitors of the β-catenin/TCF signaling pathway are structurally distinct and/or target different genes, wherein molecules targeting each gene would be

structurally distinct depending on the specific gene. Furthermore, the inhibitory molecules of claims 22, 25-29, 68, and 71-74 are each structurally distinct inhibitory molecules that act via completely different mechanisms, each requiring a separate and distinct search and corresponding examination. Further, the inhibitors do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure. Accordingly, unity of invention between the inhibitory molecules is lacking and each is considered to constitute a special technical feature. Accordingly, upon election of group I, applicant is further required to elect one antisense sequence from claim 3 for examination.

The instant sequences are considered to be each separate inventions for the following reasons: The sequences do not meet the criteria of (A), common property or activity or (B)(2), art recognized class of compounds. The sequences each behave in a different way in the context of the claimed invention. Each member of the class cannot be substituted, one for the other, with the expectation that the same intended result would be achieved. Further, the sequences do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure. Accordingly, unity of invention between the antisense sequences is lacking and each sequence claimed is considered to constitute a special technical feature. Accordingly, upon election of group I, applicant is further required to elect one antisense sequence from claim 3 for examination.

The instant sequences are considered to be each separate inventions for the following reasons: The sequences do not meet the criteria of (A), common property or activity or (B)(2), art recognized class of compounds. The sequences each behave in a

different way in the context of the claimed invention. Each member of the class cannot be substituted, one for the other, with the expectation that the same intended result would be achieved. Further, the sequences do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure. Accordingly, unity of invention between the antisense sequences is lacking and each sequence claimed is considered to constitute a special technical feature. Furthermore, each specific siRNA sequence comprises a separate and distinct sequence of nucleotides that defines for the activity of the siRNA. Each specific siRNA sequence does not contain a common structural core. Each target region of the antisense oligonucleotides defines for structurally different antisense oligonucleotides, each target region having no common core with the others. Accordingly, upon election of group IV, applicant is further required to elect an inhibitor of the β-catenin/TCF signaling pathway that targets either TC-4, β-catenin, or c-myc. Upon election of group III, IV, V, or VI, applicant is required to elect one type of inhibitory molecule from the claims. Should applicant elect "siRNA", applicant is required to elect one siRNA sequence from claim 25 for examination. Should applicant elect "dominant negative form of Prox-1 protein", applicant is required to elect one specific dominant negative form from claims 28 or 29. Should applicant elect "antisense oligonucleotide", applicant is further required to elect one target region from claims 71-73.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the

requirement may be traversed (37 CFR 1.143) and **(ii) identification of the claims encompassing the elected invention.**

The claims will be examined only to the extent to which they read on the elected invention.

The election of an invention or species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMY BOWMAN whose telephone number is (571)272-0755. The examiner can normally be reached on Monday-Thursday 6:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AMY BOWMAN
Examiner
Art Unit 1635

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